

Figure 1a

```
1  CGCGTGGGCG CGTGCAGGAA CCCGGAGCAG CCGCGCACGG ACCACAGATG
51 CGCGCGGGCTG CCGCCTGCGC TCGCAGCTGG TGCCGGTGAG TGCCTCGGC
101 CTAGGCCACA GCTCCGACGA GCTGATACGT TTCCGCTTCT GCAGCGGCTC
151 GTGCCGTCGA GCACGCTCCC AGCACGATCT CAGTCTGGCC AGCCTACTGG
201 GCGCTGGGGC CCTACGGTCG CCTCCCGGGT CCCGGNCGAT CAGCCAGCCC
251 TGCTGCCGGC CCACTCGCTA TGAGGCCGTC TCCTTCATGG ACGTGAACAG
301 CACCTGNAGG ACCGTGGACC ACCTCTCCGC CACTGCCTGC GGCTGTCTGG
351 GCTGAGGATG ATCTATCTCC AAGCCTTT
```

Figure 1b

```
smcb2-00011-d2-a      29      59      89
                        AWAAGTRSSRARTTDARGCRLRSQLVPS
                        :: ||| | ||| : || | ||| |||
SW:NRTN_MOUSE    RLAQYRALQAGAPDAVELRELSPWAAIPGPRRRAGPRRRAR-PGARPCGLRELEVRVS
                        60      70      80      90      100      110

smcb2-00011-d2-a      119      149      179      209      239      269
                        ALGLGHSSDELIRFRFCGSCRRARSQHDLSLASLLGAGALRSPPGSRPISQPCCRPTRY
                        ||| : ||| : ||| : ||| : ||| : ||| : ||| : ||| : ||| : ||| : |||
SW:NRTN_MOUSE    ELGLGYTSDETVLFRYCAGACEAAIRTYDLGLRRLRQRRVRR---ERARHPCCRPTAY
                        120      130      140      150      160

smcb2-00011-d2-a      299      329      359
                        E-AVSFMDVNSTWRTVDHLSATACGCLG*G*SISKP
                        | ||| : ||| : ||| : ||| : ||| : ||| : ||| : ||| : ||| : |||
SW:NRTN_MOUSE    EDEVSFLDVHSRYHTLQELSARECACV*
                        170      180      190
```

Figure 1c

```
1 CGGACGCGTG GCGGACGCG TGGGCGCGTG CAGGAACCCG GAGCAGCCGC
51 GCACGGACCA CAGATGCGCG CGGCTGCCGC CTGCGCTCGC AGCTGGTGCC
101 GGTGAGTGCG CTCGGCCTAG GCCACAGCTC CGACGAGCTG ATACGTTTCC
151 GCTTCTGCAG CGGCTCGTGC CGCCGAGCAC GCTCCCAGCA CGATCTCAGT
201 CTGGCCAGCC TACTGGGCGC TGGGGCCCTA CGGTGCGCTC CCGGGTCCCG
251 GCCGATCAGC CAGCCCTGCT GCCGGCCCCAC TCGCTATGAG GCCGTCTCCT
301 TCATGGACGT GAACAGCACC TGGAGGACCG TGGACCACCT CTCCGCCACT
351 GCCTGCGGCT GTCTGGGCTG AGGATGATCT ATCTCCAAGC CTTTGACAC
401 TAGACCCATG TGTTGCCCTA CCTGGAACAG CTCCACCGGG CCTCACTAAC
451 CAGGAGCCTC AACTCAGCAG GATATGGAGG CTGCAGAGCT CAGGCCCCAG
501 GCCGGTGAGT GACAGACGTC GTCGGCATGA CAGACAGAGT GAAAGATGTC
551 GGAACCACTG ACCAACAGTC CCAAGTTGTT CATGGATCAC AGCTCTACAG
601 ACAGGAGAAA CCTCAGCTAA AGAGAACTCC TCTGGGAGAA TCCAGAAATG
651 GCCCTCTGTC CTGGGGAATG AATTTTGAAG AGATATATAT ACATATATAC
701 ATTGTAGTCG CGTTGCTGGA CCAGCCTGTG CTGAAACCAG TCCCGTGTTT
751 ACTTGTTGAA GCCGAAGCCC TATTTATTAT TTCTAAATTA TTTATTTACT
801 TTGCTGGTTT GTCAGATCCT TTCCTGGACA TGGGGGATGG TAGAAGAAGC
851 TAGATGAAGA TGTGCCCCAC CCCACCCCCC CATCCACATT TTACACTTGA
901 CTCAGTAGTG CTACCTGGAT CGCCTACTTC TTGCCCCGCA GGTGTCTCTG
951 AGATGGATGG GAGGCACACA TAGGTGACAA AGATGCACAA TCCACAGTAC
1001 TTGGGGCCTG GGGTACCTAT GGGAAATAAA CAATATAGTT TTCTATGGAA
1051 AAAA
```

Figure 2

```
1   CCAAGCTTGG TACCGAGCTC GGATCCACTA GTAACGGCCG CCAGTGTGCT
51  GGAATTCGCC CTTACTCACT ATAGGGCTCG AGCGGCCGCC CGGGCAGGTA
101 TAAAAAAAAA AAGCGGCCTA GAATTCAGCG GCCGCTGAAT TCTAGGCTGC
151 CGCAGGAAGA GGGTGGGGAA ACGGGTCCAC GAAGGCTTCT GATGGGAGCT
201 TCTGGAGCCG AAAGCTATGG AACTGGGACT TGCAGAGCCT ACTGCATTGT
251 CCCACTGCCT CCGGCCTAGG TGGCAGTCAG CCTGGTGGCC AACCCTAGCT
301 GTTCTAGCCC TGCTGAGCTG CGTCACAGAA GCTTCCCTGG ACCCAATGTC
351 CCGCAGCCCC GCCGCTCGCG ACGGTCCCTC ACCGGTCTTG GCGCCCCCA
401 CGGACCACCT GCCTGGGGGA CACACTGCGC ATTTGTGCAG CGAAAGAACC
451 CTGCGACCCC CGCCTCAGTC TCCTCAGCCC GCACCCCCGC CGCCTGGTCC
501 CGCGCTCCAG TCTCCTCCCG CTGCGCTCCG CGGGGCACGC GCGGCGCGTG
551 CAGGAACCCG GAGCAGCCGC GCACGGACCA CAGATGCGCG CGGCTGCCGC
601 CTGCGCTCGC AGCTGGTGCC GGTGAGCGCG CTCGGCCTAG GCCACAGCTC
651 CGACGAGCTG ATACGTTTCC GCTTCTGCAG CGGCTCGTGC CGCCGAGCAC
701 GCTCCCAGCA CGATCTCAGT CTGGCCAGCC TACTGGGCGC TGGGGCCCTA
751 CGGTCGCCTC CCGGGTCCCG GCCGATCAGC CAGCCCTGCT GCCGGCCCAC
801 TCGCTATGAG GCCGTCTCCT TCATGGACGT GAACAGCACC TGGAGGACCG
851 TGGACCACCT CTCCGCCACT GCCTGCGGCT GTCTGGGCTG AGGATGATCT
901 ATCTCCAAGC CTTTGACAC TAGACCCATG TGTTGCCCTA CCTGGAACAG
951 CTCCAAGGGC GAATTCTGCA GATATCCATC AACTGGCGG CCGCTCGAGC
1001 ATGCATCTAG AGG
```

Figure 3

1 MELGLAEPTA LSHCLRPRWQ SAWWPTLAVL ALLSCVTEAS LDPMSRSPAA
51 RDGPSPVLAP PTDHLPGGHT AHLCSERTLR PPPQSPQPAP PPPGPALQSP
101 PAALRGARAA RAGTRSSRAR TTDARGCRLR SQLVPVSALG LGHSSDELIR
151 FRFCSGSCRR ARSQHDLSLA SLLGAGALRS PPGSRPISQP CCRPTRYEAV
201 SFMDVNSTWR TVDHLSATAC GCLG*

Neurturin	10	20	30	40
	MRRMKAALVSLICSSLLSVMMC-QEGLLGHRLGPAL----	APL		
Grf4	10	20	30	40
	MELGLAEPTALSHCLRPWQSAWPTLAVLALLS---CVTEASLDPMRSRSPAARDGSPSPV			
Neurturin	50	60	70	80
	RRPRTL--DARIARLAQVRALL-----QGAPDAVELRELSPWAARIPGPRR-RAGPRR			
Grf4	60	70	80	90
	LAPPTDHLPGGHTAHLCSERTLRPPQPSPQAPPPPGPALQSPAA-LRGARAARAGTRS			
Neurturin	100	110	120	130
	RRAP-GARPCGLRELVRSVSELGYTSDETVLFYRCAGACEAAIRIYDLGLRRLRQR			
Grf4	120	130	140	150
	SRARTDARGCRLRSQLPVPSALGLHSSDELIRFRFCGSCRRARSQHDLSLASLLGAG			
Neurturin	160	170	180	190
	RVRRE---RARAHPCCRPATAYEDEVSFLDVHSRVHTLQELSARECACV*			
Grf4	160	170	180	190
	ALRSPPGSRPIQPCCRPTRYE-AVSFMDVNSTWRTVDHLSATACGCLG*			

Figure 5

ClustalW Formatted Alignments

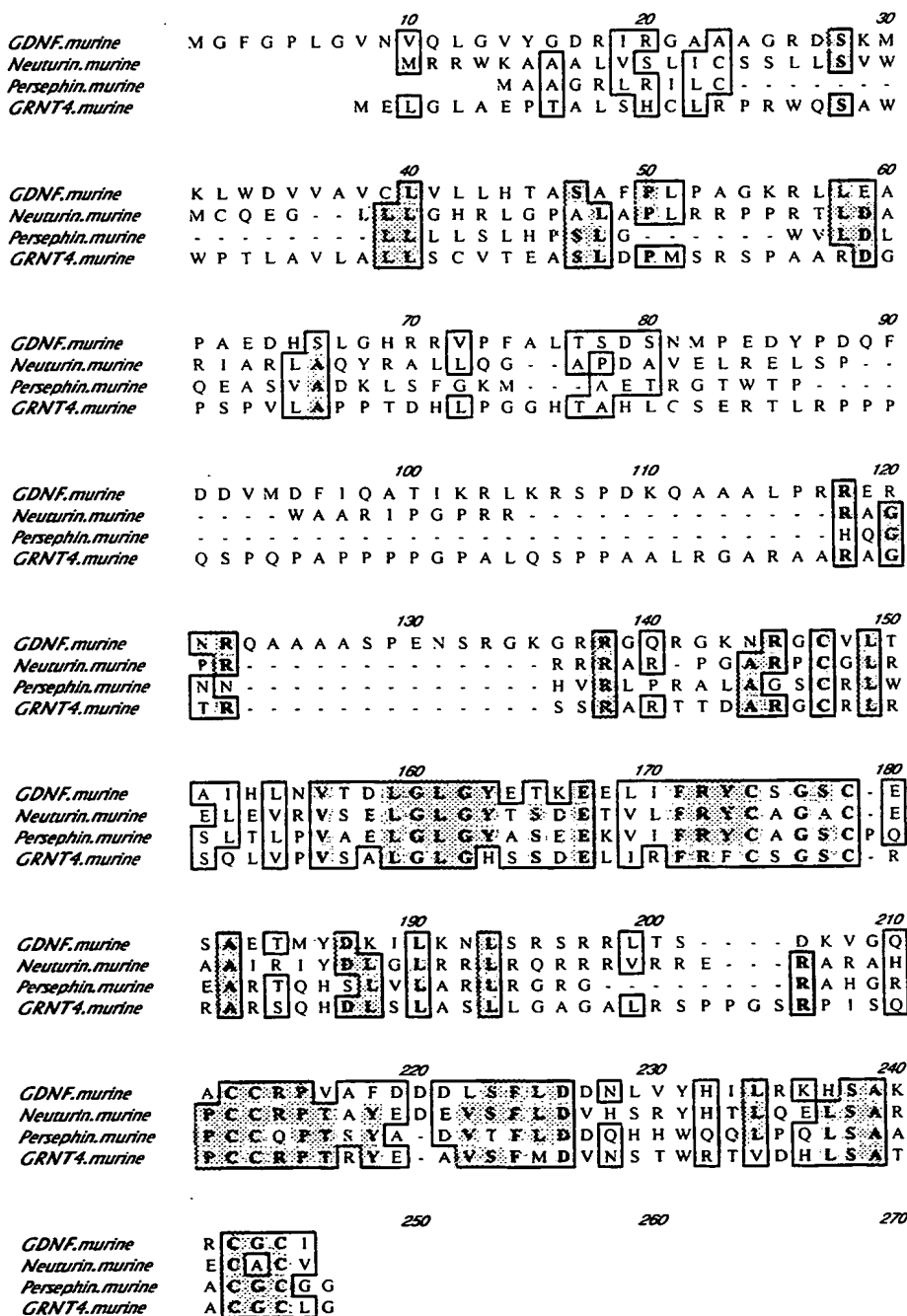


Figure 6

```
1  CAACAATGGC TGATGGGCGC TCCTGGTGTT GATAGAGATG GAACTTGGAC
51  TTGGAGGCCT CTCCACGCTG TCCCACTGCC CCTGGCCTAG GCGGCAGGCT
101 CCACCTGGTC TCTCCGCGCA GCCTGCCCTG TGGCCACCC TGGCCGCTCT
151 GGCTCTGCTG AGCAGCGTCG CAGAGGCCTC CCTGGGCTCC GCGCCCCGCA
201 GCCCTGCCCC CCGCGAAGGC CCCCCGCTG TCCTGGCGTC CCGCGCCGGC
251 CACCTGCCGG GGGGACGCAC GGCCCGCTGG TGCAGTGGAA GAGCCCGGCG
301 GCGCGCCCGG CAGCCTTCTC GGCCCGCGCC CCGCGCGCCT GCACCCCCAT
351 CTGCTCTTCC CCGCGGGGGC CGCGCGGCGC GGGCTGGGGG CCGGGGCAGC
401 CGCGCTCGGG CAGCGGGGGC GCGGGGCTGC CGCCTGCGCT CGCAGCTGGT
451 GCCGGTGCGC GCGCTCGGCC TGGGCCACCG CTCCGACGAG CTGGTGCGTT
501 TCCGCTTCTG CAGCGGCTCC TGCCGCCGCG CGCGCTCTCC ACACGACCTC
551 AGCCTGGCCA GCCTACTGGG CGCCGGGGCC CTGCGACCGC CCGGGGCTC
601 CCGGCCCCGC AGCCAGCCCT GCTGCCGACC CACGCGCTAC GAAGCAGTCT
651 CCTTCATGGA CGTCAACAGC ACCTGGAGAA CCGTGGACCG CCTCTCCGCC
701 ACCGCCTGCG GCTGCCTGGG CTGAGGGCTC GCTCCA
```


Figure 7

1 MELGLGGLST LSHCPWPRRQ APLGLSAQPA LWPTLAALAL LSSVAEASLG
51 SAPRSPAPRE GPPPVLASPA GHLPGGRTAR WCSGRARRPP PQPSRPAPPP
101 PAPPSALPRG GRAARAGGPG SRARAAGARG CRLRSQ LVPV RALGLGHRSD
151 ELVRFRFCSG SCRRARSPHD LSLASLLGAG ALRPPPGSRP VSQPCCR PTR
201 YEAVSFMDVN STWRTVDRLS ATACGCLG*

Figure 8

```
mouse      1 MELGLAEPTALSHCLRPRWQS.....AWWPTLAVLALLSCVTEASLD 42
          ||||| . ||||| |||. ||||| ||||| ||||| |||||
human      1 MELGLGGLSTLSHCPWPRRQAPLGLSAQPALWPTLAALALLSSVAEASLG 50
          ||||| : ||||| ||||| ||||| ||||| ||||| |||||
mouse     43 PMSRSPAARDGSPFVLAPPTDHLPGGHTAHLCSERTLRPPPQSPQPAPPP 92
          ||||| : ||||| ||||| ||||| ||||| ||||| |||||
human     51 SAPRSPAPREGPPPVLASPAHLPGGRTARWCSGRARRPPPQPSRPAPPP 100
          ||||| : ||||| ||||| ||||| ||||| ||||| |||||
mouse     93 PGPALQSPPAALRGARAARAGTRSSRARTTDARGCRLRSQLVVPVSALGLG 142
          ||||| : ||||| ||||| ||||| ||||| ||||| |||||
human    101 PAP...PSALPRGGRAARAGGPGSRARAAGARGCRLRSQLVVPRALGLG 146
          ||||| : ||||| ||||| ||||| ||||| ||||| |||||
mouse    143 HSSDELIRFRFCGSGCRRARSQHDLASLLGAGALRSPPGSRPISQPCC 192
          ||||| : ||||| ||||| ||||| ||||| ||||| |||||
human    147 HRSDELVRFRFCGSGCRRARSPHDLASLLGAGALRPPPGSRPVSPQCC 196
          ||||| : ||||| ||||| ||||| ||||| ||||| |||||
mouse    193 RPTRYEAVSFMDVNSTWRTVDHLSATACGCLG* 225
          ||||| ||||| ||||| ||||| ||||| ||||| |||||
human    197 RPTRYEAVSFMDVNSTWRTVDRLSATACGCLG* 229
          ||||| ||||| ||||| ||||| ||||| ||||| |||||
```

Figure 9

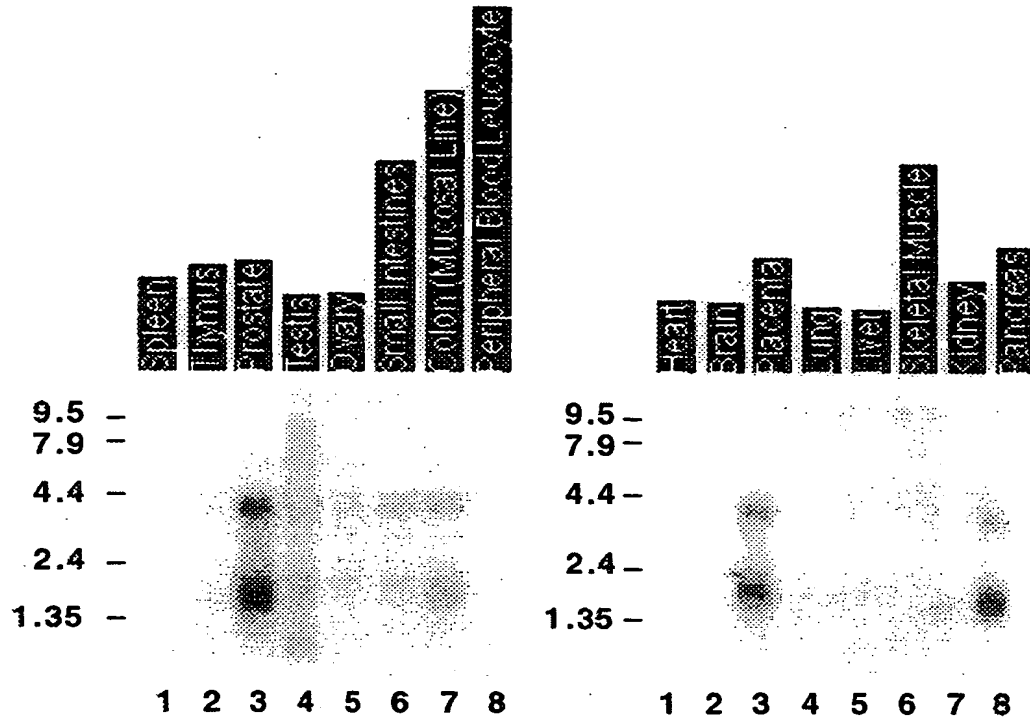


Figure 10

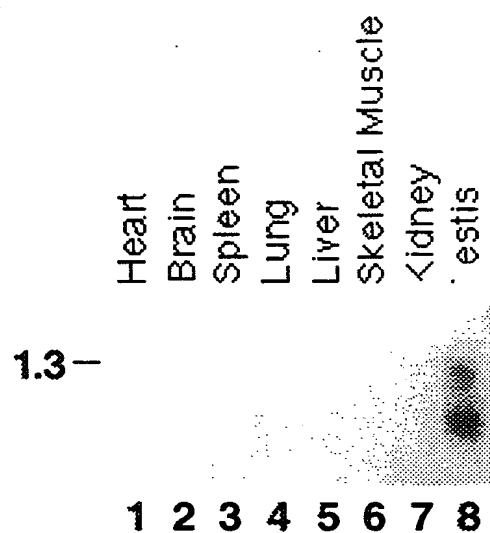


Figure 11



Figure 12

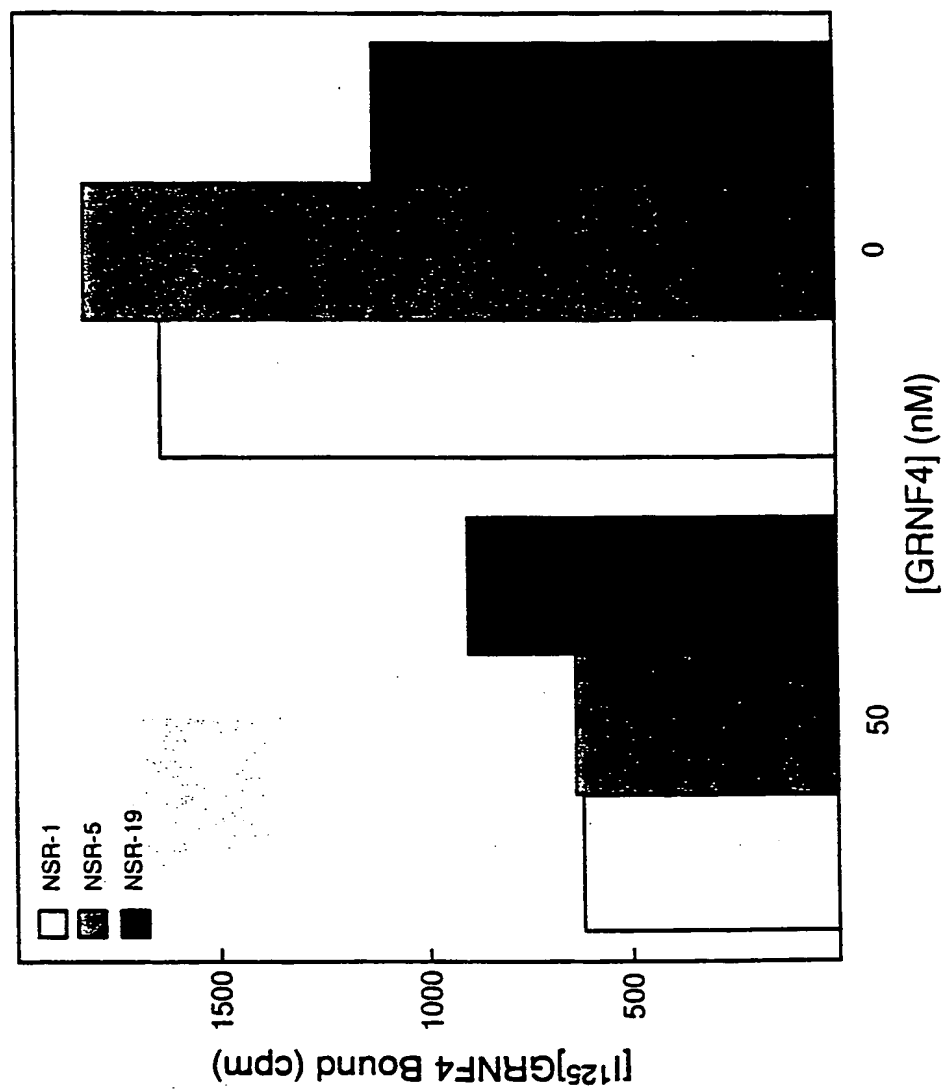


Figure 13

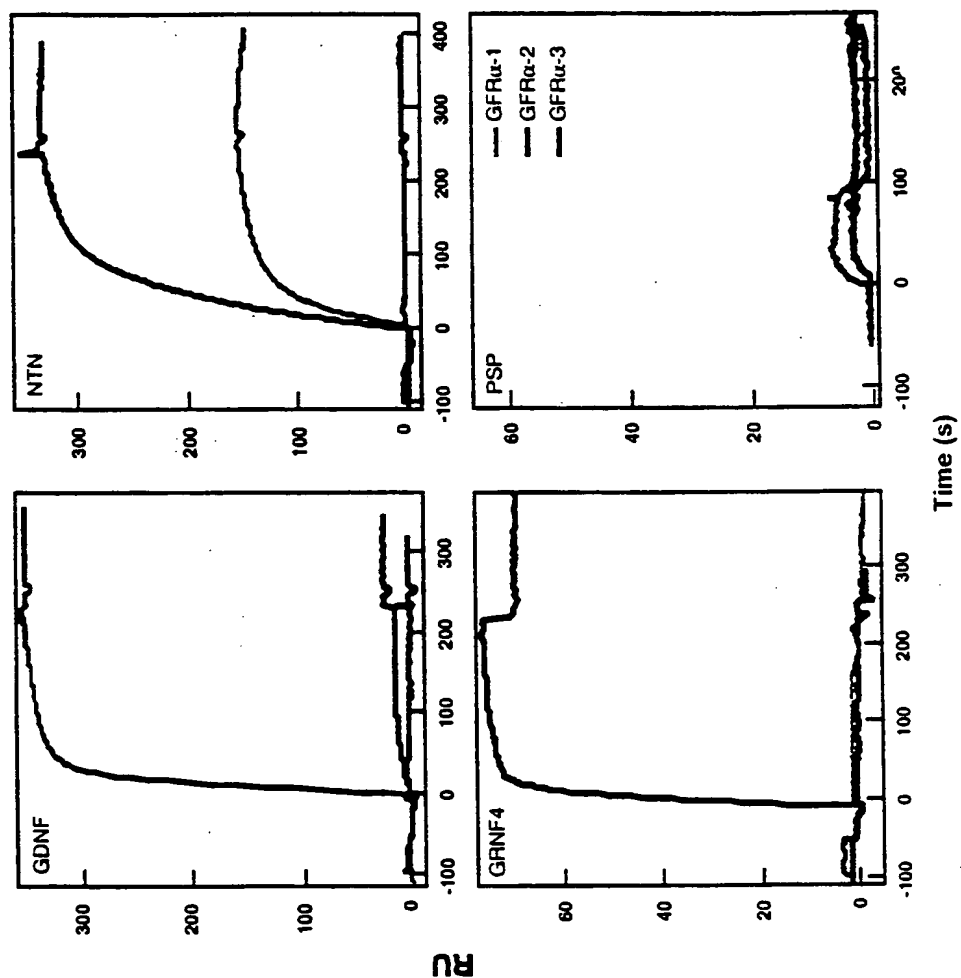
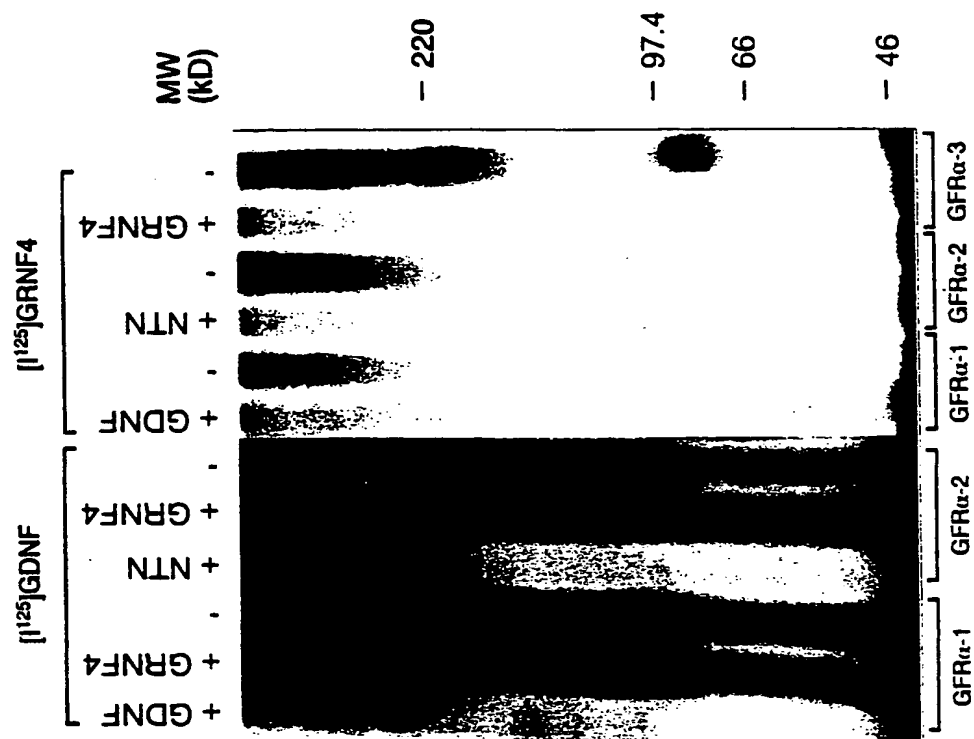


Figure 14



GRNF4						
+	-	+	-	+		
					MW (kD)	
					- 220	
					- 200	
					- 97.4	
					- 66	
					- 46	
NGR-38			NNR-9			NSR-5

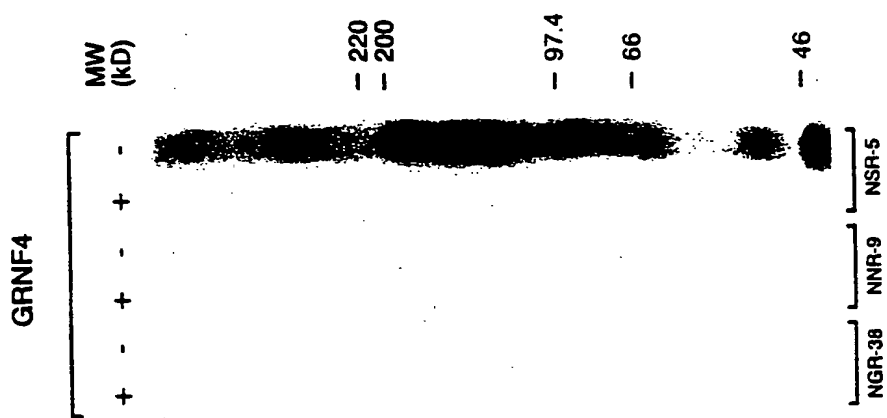


Figure 16

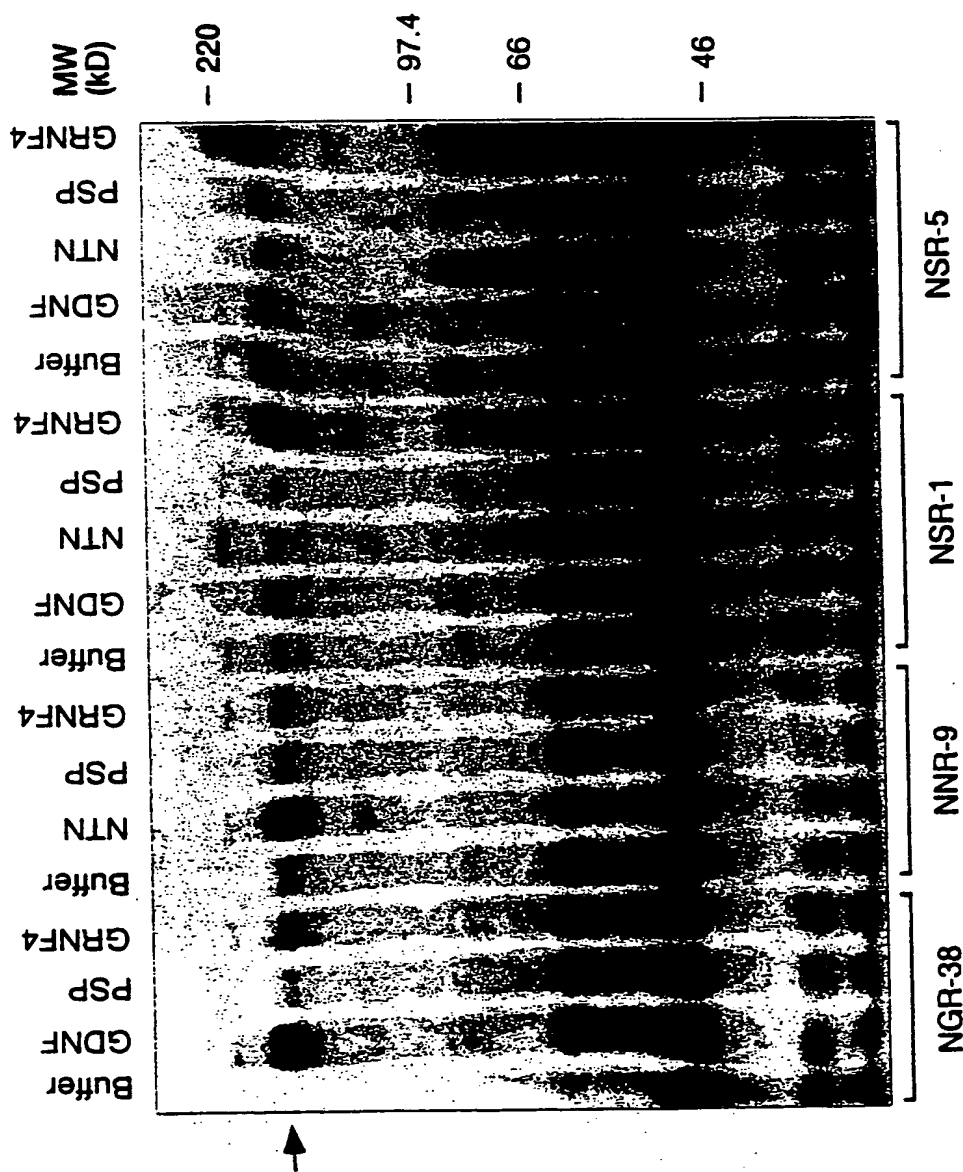


Figure 17

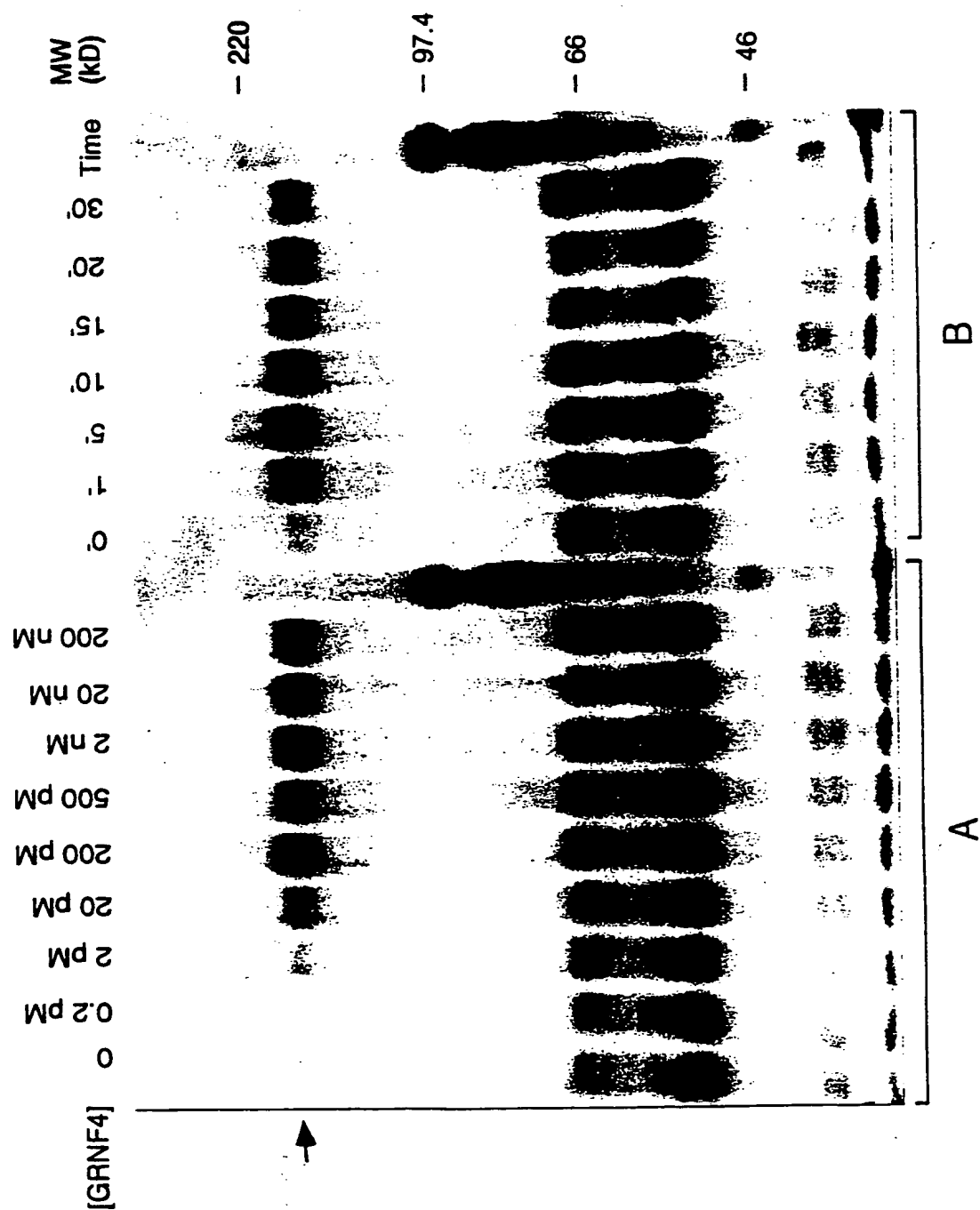


Figure 18

M E L G L (Xaa)₅ L S H C (Xaa)₂ P R (Xaa)_{0.4} (Xaa) Q (Xaa) A (Xaa) W P T L
A (Xaa) L A L L S (Xaa) V (Xaa) E A S L (Xaa)₄ R S P A (Xaa) R (Xaa) G P
(Xaa) P V L A (Xaa) P (Xaa)₂ H L P G G (Xaa) T A (Xaa)₂ C S (Xaa) R (Xaa)₂
R P P P Q (Xaa)₃ P A P P P P (Xaa) P (Xaa)₄ P (Xaa)_{0.4} R G (Xaa) R A A R A
G (Xaa)₃ S R A R (Xaa)₃ A R G C R L R S Q L V P V (Xaa) A L G L G H (Xaa)
S D E L (Xaa) R F R F C S G S C R R A R S (Xaa) H D L S L A S L L G A G A
L R (Xaa) P P G S R P (Xaa) S Q P C C R P T R Y E A V S F M D V N S T W R
T V D (Xaa) L S A T A C G C L G

Figure 19

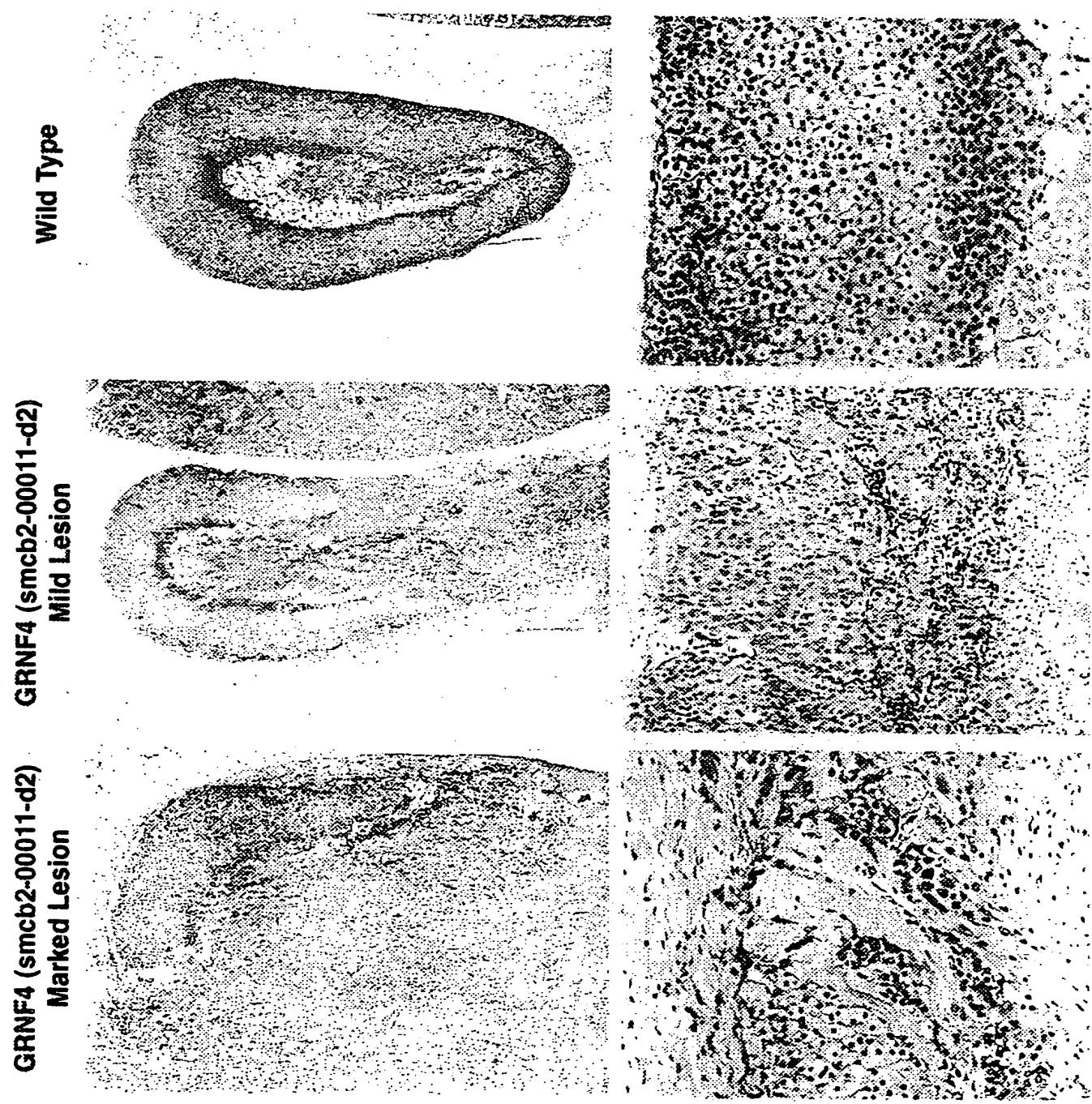


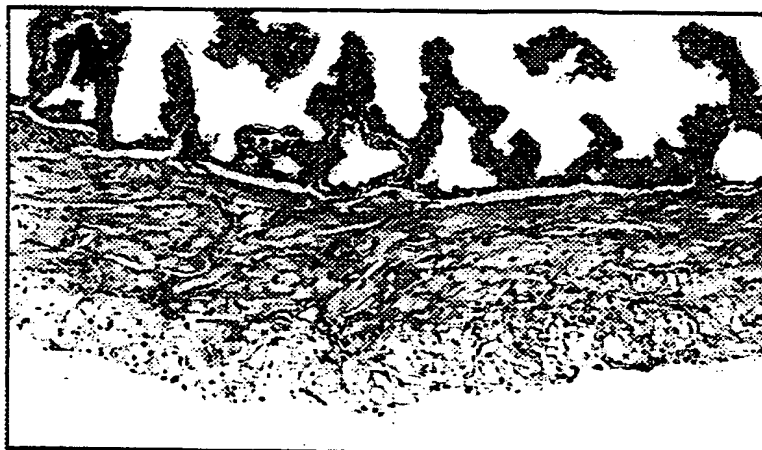
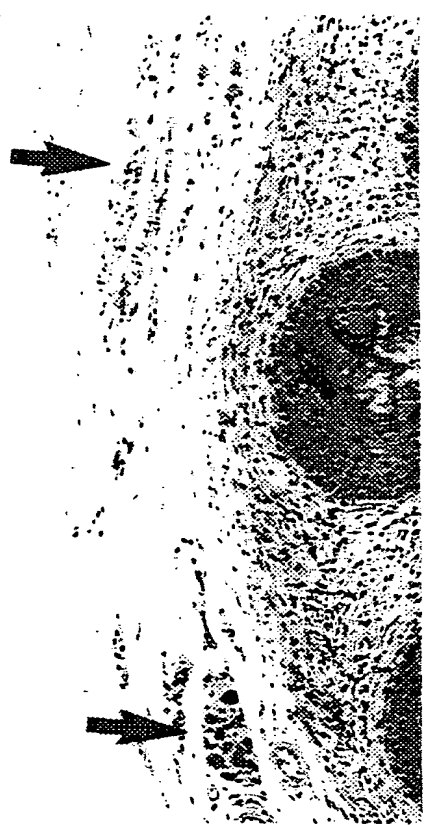
Figure 20**Wild Type****smcb2-00011-d2****smcb2-00011-d2**

Figure 21

Wild Type



smcb2-00011-d2

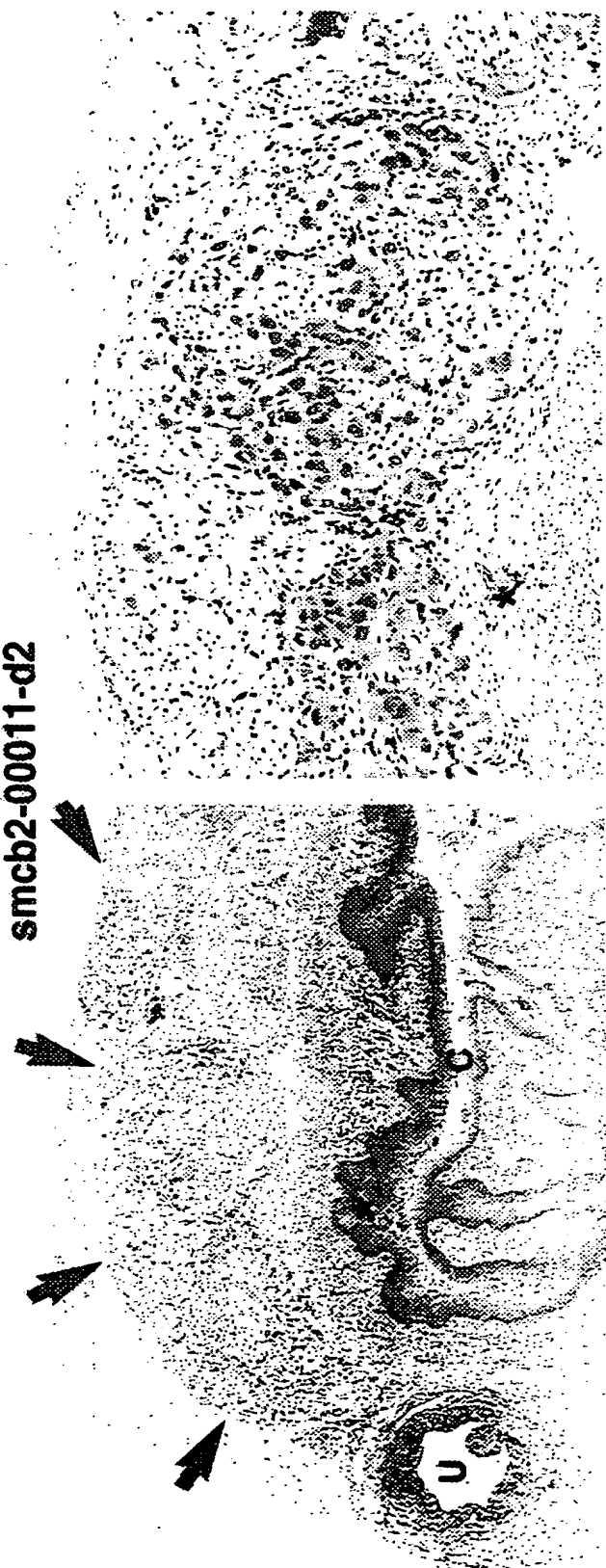


Figure 22**Wild Type****smcb2-00011-d2**